Cytoskeleton

Made of proteins
Dynamic properties
Coordinate with each other
Coordinate with external signal
# Biological functions of the cytoskeleton

<table>
<thead>
<tr>
<th>Tissue level</th>
<th>Cell level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Muscle movement</td>
<td>Cell shape</td>
</tr>
<tr>
<td></td>
<td>Cell movement</td>
</tr>
<tr>
<td></td>
<td>Cell adhesion</td>
</tr>
<tr>
<td></td>
<td>Mitosis</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Subcellular level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intracellular movement of vesicles</td>
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<tr>
<td>Location of subcellular organelles</td>
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<tr>
<td>Organizing cell polarity</td>
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<tr>
<td>Endocytosis – clathrin-mediated endocytosis and phagocytosis</td>
</tr>
</tbody>
</table>
Actin cytoskeleton

- G-actin
  - ATP-binding cleft
  - C-terminus
  - N-terminus
  - Mg++

- F-actin

(c) (-) end

(+ end)
Microtubule

(a) α-Tubulin β-Tubulin

GTP GDP Taxol

Non exchangeable Exchangeable

α-Tubulin GTP GDP β-Tubulin

Protofilament

8 nm 24 nm
Polymerization of G-actin

(a) G-actin → Nucleus → F-actin

(b) + nuclei → − nuclei

(b) Time

Mass of filaments

Mass

Filament

Monomer

Actin concentration

$C_c$
Treadmilling of actin filaments

$C^{-}_c > \text{G-actin concentration} > C^{+}_c$

$c_c – \text{Critical concentration}$
Assembly of microtubules

1. Protofilament assembly
2. Sheet assembly
3. Microtubule elongation

MT: Microtubule
Flagellar nucleus
β-Tubulin
α-Tubulin
GTP
GDP
(+)-end
(−)-end
GTP cap
GTP microtubule
α-Tubulin
β-Tubulin
Dynamic instability of microtubules
Organization of the actin cytoskeleton
Protein involved in the actin cytoskeleton organization

(a) Actin filament

(b) Filamin cross-linker

36 nm
Regulation of actin polymerization
Figure 3. Dendritic Nucleation/Array Treadmilling Model for Protrusion of the Leading Edge

1. Extracellular signals activate receptors.
2. The associated signal transduction pathways produce active Rho-family GTPases and PIP2 that
3. activate WASp/Scar proteins.
4. WASp/Scar proteins bring together Arp2/3 complex and an actin monomer on the side of a preexisting filament to form a branch.
5. Rapid growth at the barbed end of the new branch (6) pushes the membrane forward.
6. Capping protein terminates growth within a second or two.
7. Filaments age by hydrolysis of ATP bound to each actin subunit (white subunits turn yellow) followed by dissociation of the γ phosphate (subunits turn red).
8. ADF/cofilin promotes phosphate dissociation, severs ADP-actin filaments and promotes dissociation of ADP-actin from filament ends.
9. Profilin catalyzes the exchange of ADP for ATP (turning the subunits white), returning subunits to (11) the pool of ATP-actin bound to profilin, ready to elongate barbed ends as they become available.
10. Rho-family GTPases also activate PAK and LIM kinase, which phosphorylates ADF/cofilin. This tends to slow down the turnover of the filaments. (Redrawn from a figure in Pollard et al., 2000). Reprinted with permission from the Annual Review of Biophysics and Biomolecular Structure, Volume 29, copyright 2000 by Annual Reviews, www.annualreviews.org.
Centrosome - a microtubule-organization center

C, centrioles; PC, pericentriolar matrix,
Orientation of cellular microtubules

(a) Interphase animal cell
- Basal body
- Flagellum or cilium
- Nucleus
- Centriole
- MTOC

(b) Mitotic animal cell
- Chromosome
- MTOC
- Centriole
- Spindle microtubule

(c) Nerve cell
- Dendrite
- Axon
- MTOC
- Nucleus
- Cell body
The $\gamma$-tubulin ring complex is localized to one end of the microtubule.
Motors of the actin filaments

<table>
<thead>
<tr>
<th>Type</th>
<th>Heavy Chain (MW)</th>
<th>Structure</th>
<th>Step Size (nm)</th>
<th>Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>110,000–150,000</td>
<td><img src="image1.png" alt="Structure Image" /></td>
<td>10–14</td>
<td>Membrane binding, endocytic vesicles</td>
</tr>
<tr>
<td>II</td>
<td>220,000</td>
<td><img src="image2.png" alt="Structure Image" /></td>
<td>5–10</td>
<td>Filament sliding</td>
</tr>
<tr>
<td>V</td>
<td>170,000–220,000</td>
<td><img src="image3.png" alt="Structure Image" /></td>
<td>36</td>
<td>Vesicle transport</td>
</tr>
<tr>
<td>VI</td>
<td>140,000</td>
<td><img src="image4.png" alt="Structure Image" /></td>
<td>30</td>
<td>Endocytosis</td>
</tr>
<tr>
<td>XI</td>
<td>170,000–260,000</td>
<td><img src="image5.png" alt="Structure Image" /></td>
<td>35</td>
<td>Cytoplasmic streaming</td>
</tr>
</tbody>
</table>
Functions of myosin tail domains

Relaxed

![Diagram showing the relaxed state of myosin II tails, bare zone, actin, myosin, and relaxed bands (I band and A band)].

Contracted

![Diagram showing the contracted state of myosin II tails, bare zone, actin, myosin, and contracted bands (I band and A band)].

+ ATP, Ca^{2+}
Kinesins (+) end-directed microtubule motors
Kinesin-catalyzed vesicle transport
Dynein (-) end-directed microtubule motors
Actin-mediated cell migration
Actin-mediated movement of *Listeria* in infected fibroblasts
ER

microtubules
Flagella-mediated movement

Sperm

Chlamydomonas
Cooperation of myosin and kinesin at cell cortex